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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/249,011	02/12/1999	MAN SUNG CO	GI-5315	9459

7590 11/25/2002

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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	21

DATE MAILED: 11/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/249011	CO :
Examiner	**Art Unit**
GAMBEL	1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application. 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-48, 51-76

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 41-45, 47, 48, 51-63

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected. 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-40, 46, 64-76

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 9/28/00 is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

PAPER NO 31

DETAILED ACTION

1. The request filed 6/20/02 (Paper No. 26) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/249,011 is acceptable and a CPA has been established An Office Action on the CPA follows.

Applicant's amendment, filed 8/28/02 (Paper No. 27), has been entered.
Claims 1, 2, 8, 15, 21, 25, 30, 33, 40 and 75 have been amended.

Claims 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-40, 46 and 64-76 are being considered as the elected invention.

Claims 41-45, 47,48, 51-63 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to nonelected invention and/or species

Claims 13-14, 16-20, 22, 26, 29, 37 and 49-50 have been canceled previously

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 8/28/02 (Paper No. 27)
The rejections of record can be found in the previous Office Actions (Paper Nos. 14/18/22).

3. Formal drawings, filed 8/28/02, have been submitted which comply with 37 CFR 1.84.

4. Claims 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-40, 46 and 64-76: It is apparent that the "3D1" and "H2F", "I2R" antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell lines/hybridomas which produces these antibodies. See 37 CFR 1.801-1.809.

Applicant has argued that the prior art antibodies are known and available to the public; given that CRL-12524 cell line was deposited with the ATCC; that the 3D1 is available from the ATCC, as indicated in U.S. Patent No. 6,084,067 and H2F and I2R antibodies were disclosed in Manheimer-Lory (J. Exp. Med. 174: 1639-1652, 1991)

However as previously noted, biological materials must be known and readily available to the public (See MPEP 2404.01). Neither concept alone is sufficient. The fact that applicant and other members of the public were able to obtain the materials in question from a given depository prior to and after the filing date of the application does not establish the upon issuance of a patent on the application that such material would continue to be accessible to the public. The applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials from the depository, nor is there any evidence as to the depository's policy regarding the material if a patent would be granted. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent. In the absence of evidence that the "3D1", "H2F" and "I2R" antibodies / hybridomas are readily available to the public and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, applicant's arguments are not persuasive and the rejection is maintained.

It was noted that the mere reference to a deposit or the biological material itself in any document or publication does not necessarily mean that the deposited biological material is readily available. Even a deposit made under the Budapest Treaty and referenced in a United States or foreign patent document would not necessarily meet the test for known and readily available unless the deposit was made under conditions that are consistent with those specified in these rules, including the provision that requires, with one possible exception, that all restrictions on the accessibility be irrevocably removed by the applicant upon the granting of the patent. Ex parte Hildebrand , 15 USPQ2d 1662 (Bd Pat. App. & Int. 1990). See MPEP 2404.01

With respect to applicant's previous comments that these materials are obtainable by a repeatable methods set forth in the specification; given the high polymorphism of antibodies; the skilled artisan could not predict the sequence of the claims specific 3D1, H2F and I2R antibodies by simply relying upon the disclosed methods steps.

As pointed out previously, in addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Again, as pointed out previously, it has been noted that if the claimed and disclosed amino acid sequences or nucleic acid sequences set forth in the instant application encode the entire "3D1", "H2F" and "I2R" antibodies; then a deposit for said "antibodies (cell lines/hybridomas) are not required. The sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin.

Applicant's arguments and comments, filed 8/28/02 (Paper No. 27), have been fully considered but are not found convincing for the reasons of record and that set forth herein.

The 3D1 Antibody

Application submission of the entire nucleotide and amino acid sequences for the 3D1 antibody in paper form, thereby making the antibody available to the public.

However, the application as-filed did not provide support for the entire nucleotide and amino acid sequence of the 3D1 antibody. Therefore, applicant cannot rely upon information not supported by the specification as-filed to provide essential material to enable the claimed invention.

It appears that the application as-filed provides for the sequences of the variable (Figures 1A-B, 2A-B) but not the constant regions of the humanized and murine 3D1 antibodies.

Alternatively, it does not appear that the 3D1 antibody has been deposited under the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

The I2R (III2R) and H2F Antibodies

Applicant's reliance on the availability of the sequences for the III2R and H2F antibodies in Manheimer-Lory, J. Exp. Med. 174: 1639-1652 (1991) is acknowledged.

However, it appears that applicant is attempting to incorporate essentially subject matter by reference to a publication.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. Ex parte Schwarze, 151 USPQ 426 (Bd. of Appeals, 1966). an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or application published by the United states or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications or (3) non-patent publications, for purposes of indicating the background of the invention or illustrating the state of the art.

The referencing application must include (1) an abstract, (2) a brief summary of the invention, (3) an identification of the referenced patent or application, (4) at least one view in the drawing in those applications admitting of a drawing, and (5) one or more claims. Particular attention should be directed to specific portions of the referenced patent or application.

If supported by the specification as-filed, applicant is invited to consider providing the sequences of the III2R and H2F antibodies and amending the specification and Sequence Listing accordingly.

Applicant is reminded of the Sequence Rules for application which contain sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825.

Applicant is also reminded of providing a Hawkins Declaration stating that the amendatory material consists of the same material incorporated by reference in the referencing application and that no new matter is being amended.

Applicant's comments on the construction of the chimeric and humanized 3D1 antibodies disclosed in the specification as-filed are acknowledged.

Although applicant asserts that the III2R and H2F antibodies themselves were never physically used as reagents and that it is not necessary for the entire amino acids of these antibodies and hybridomas that produced these antibodies to be disclosed, the claims recite 3D1, III2R and H2F as reference or starting materials in the claimed invention. Therefore, the 3D1, III2R and H2F antibodies (and/or hybridomas) are required to practice the claimed invention and are considered essential to the claimed invention.

Therefore, applicant must provide the sequences in compliance with the Sequence Rules and/or deposit the appropriate biological materials to satisfy the enablement requirements under 35 USC 112, first paragraph in order for the skilled artisan to make and use the claimed invention.

Again applicant is invited to consider incorporation by reference or the deposit of the appropriate biological materials as indicated above and of record. Applicant is reminded that the specification as-filed must provide adequate support if applicant intends to amend the application to bring in sequences not disclosed in the application as-filed to avoid new matter considerations.

The Ryan Declaration under 37 C.F.R. § 1.132 has satisfied the requirements for the deposit of biological materials under 35 USC 112, first paragraph.

5. Claims 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-40, 46 and 64-76 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-40, 46 and 64-76 are indefinite in the recitation of "3D1" and "H2F", "I2R" antibodies because their characteristics are not known. The use of "3D1" and "H2F", "I2R" antibodies" as the sole means of identifying the claimed antibodies renders the claims indefinite because these "names" are merely laboratory designations which do not clearly define the claimed products; since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas.

As pointed out above; the disclosure of the sequence for an entire immunoglobulin satisfies the biological deposit of said immunoglobulin and amending the claims to incorporate the appropriate SEQ ID NOS. would render the claims definite.

Applicant's arguments have been fully considered, but are not found convincing essentially for the reasons of record.

Applicant's reliance upon the 3D1, H2F and I2R disclosed in the specification and in U.S. Patent No. 6,084,067 and Manheimer-Lory et al. (J. Exp. Med. 174: 1639-1652, 1991) antibody is acknowledged.

As pointed out in the last Office Action, the use of "3D1" and "H2F", "I2R" antibodies" as the sole means of identifying the claimed antibodies renders the claims indefinite because these "names" are merely laboratory designations which do not clearly define the claimed products; since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas. There are many subjective and objective characteristics that can be associated with an antibody, including the 3D1" and "H2F", "I2R" antibodies. In addition, a particular biological cell line such as a hybridoma can undergo changes resulting in microheterogeneity in the products such as antibodies that such cell lines can reproduce. To obviate any ambiguity as to whether the designations 3D1" and "H2F", "I2R" antibodies refers to a particular characteristic (e.g. B7-2-specificity) , to a particular set of characteristics (e.g. structural and/or functional) or to a particular cell line (e.g. ATCC HB 11686) and all of its corresponding characteristics; the recitation of the deposit cell line is required. The 3D1" and "H2F", "I2R" designations are an incomplete and ambiguous description of the biological materials in the absence of the appropriate deposit accession numbers . It is not clear why applicant does not want to recite the appropriate ATCC

accession number in conjunction with 3D1" and "H2F", "I2R" antibodies, unless these "designations" are intended to mean something other than the particular antibodies produced by the particular deposited hybridomas. Applicant's arguments are not found persuasive and the rejection is maintained.

Applicant's arguments, filed 8/28/02 (Paper No. 27), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the sequences of the 3D1 have been provided and that it is not necessary for the public to know the complete characteristics for the H2F and III2R antibodies because the framework regions were disclosed in Manheimer-Lory.

However, the claims must particularly point out and distinctly claim the subject matter which applicant regards as the invention. For the reasons of record and reiterated herein, the claims should provide either the sequence or the appropriate deposit accession number that corresponds to the claimed biological materials.

Applicant's arguments are not found persuasive.

B) Claims 24, 28 are indefinite in the recitation of " stringent conditions" because the metes and bounds of such conditions are ambiguous and unclear and, in turn, the metes and bounds of the claimed "nucleic acids" are not defined.

Applicant's arguments, filed 8/28/02 (Paper No. 27), have been fully considered but are not found convincing essentially for the reasons of record

Applicant reliance on "stringent hybridization conditions" in Ausubel et al. Eds., Current Protocols in Molecular Biology, Greene Publishing Associates and John Wiley and Sons Inc. (1993) is acknowledged. However, the citation of page 27, paragraph 2 of the instant specification discloses this reference in the context of constructs or expression vectors suitable for the expression of a humanize immunoglobulins having binding specificity and not for "hybridization conditions". Applicant is reminded that to incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where the material is found in the various documents. See Advanced Display Systems, Inc. v. Kent State Univ., 54 USPQ2d 1673 (Fed. Cir. 2000) citing In re Seversky, 177 USPQ 144, 146 (CCPA 1973). The specification as filed does not provide sufficient written description for the direction to this reference for "stringent conditions".

Again, applicant submits that "stringent hybridization conditions" was an art recognized term at the time the invention was made and therefore one of skill in the art would have known what applicant regarded as the invention with respect to this term.

In contrast to applicant's assertions; the metes and bounds of "stringent hybridization conditions" are not clearly defined. The term in clam is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

It is noted that applicant's reliance on Ausubel et al. refers to "high stringency conditions" employing "two wash buffers, while the claims are drawn to any "stringent hybridization conditions", wherein the metes and bounds are ill-defined and ambiguous.

Again, applicant is invited to point out a definition for "stringent conditions" in the specification as filed; if one is available rather than relying upon asserted definitions.

Alternatively, applicant has been invited to consider amending the claims to recite functional language as well.

C) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

7. Claims 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-40, 46 and 64-76 are rejected under 35 U.S.C. § 103 as being unpatentable over Freeman et al.. (U.S. Patent No. 6,084,067) in view of art known gene cloning and expression strategies for deriving recombinant antibodies and fragments thereof, as disclosed/admitted on pages 10-29 or Examples I (only indicated as Exemplification on page 35 of the specification/ II/III of the instant specification or as cited by references on the 1449, as evidenced by Queen et al. (U.S. Patent No. 5,585,089)(1449; #AB) and as evidenced by Harlow and Lane (Eds., Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory 1988, Chapter 3, pages 23-35). It would have been have been a matter of routine experimentation well within the ordinary skill level of art to generate chimeric, humanized or recombinant HF2.3D1-/B7-2-specific antibodies, nucleic acids encoding said antibodies, vectors, host cells, methods of making and compositions thereof; given the HF2.3D1 antibody and hybridoma and its associated properties known in the prior art. The instant claims are drawn to HF2.3D1-/B7-2-specific antibodies and fragments thereof and nucleic acids encoding said antibodies, particularly the 3D1/B7-2 specificity.

Applicant's arguments and comments, filed 8/28/02 (Paper No. 27), have been fully considered but are not found convincing for the reasons of record and that set forth herein

Applicant's arguments and the examiner's rebuttal of record are set forth in the previous Office Action (Paper No. 18).

Applicant argues that the binding affinity of ate least about 10^7 M^{-1} is comparable tot he that of the native antibody, which is not commonly known to the one of ordinary skill in the art.

Applicant in combination with certain references asserts that the art recognized that the prior humanized antibodies generally lost much of their binding specificity.

In contrast to applicant's assertions, Queen et al. teach the improved methods of humanizing antibodies of interest with binding affinities of at least about 10^8 M^{-1}, preferentially 10^9 M^{-1} to 10^{10} M^{-1} or stronger (see entire document, including the first paragraph of the Detailed Description of the Invention on column 10). Queen et al. also the same or nearly the same methods of generating humanized antibodies with the reliance on computer modeling and modifications to the framework to select for antibodies of sufficient or high affinity for the antigen of interest at the time the invention was made (see Detailed Description of the Invention).

Also, it is noted that Harlow and Lane disclose that 10^7 M^{-1} is considered a weak signal in comparison to affinities of 10^8 M^{-1} or higher (see Table 3.1 on page 28).

Given the motivation and expectation of success in generating antibodies, including diagnostic and therapeutic antibodies to antigens of interest, including B7-2, as taught by Freeman; one of ordinary skill in the art would have had a reasonable expectation of success and motivation in generating antibodies of sufficient affinity binding, including affinities of at least about 10^8 M^{-1}, preferentially 10^9 M^{-1} to 10^{10} M^{-1} or stronger, as taught by Queen et al., to achieve such endpoints or therapeutic goals.

The following of record is reiterated for applicant's convenience.

In contrast to applicant's assertions, it appears that applicant has relied upon the selection of the I2R and H2F framework modifications of the B7-2-specific humanized antibodies based upon the B7-2-specific 3D1 antibody, as disclosed in Example 2 of the instant specification.

For example, page 37, paragraph 1 discloses that the "The computer programs ABMOD and ENCODE (Levitt et al. J. Mol. Biol. 168: 595 (1983)) were used to construct a molecular model of the 3D1 variable domain which was used to locate the amino acids in the 3D1 framework that are close enough to the CDRs to potentially interact with them. To design the humanized 3D1 heavy and light chain variable regions, the CDRs from the mouse 3D1 heavy chain were grafted into the framework regions of the human I2R heavy chain and the CDRs from the mouse 3D1 light chain grafted into the framework regions of the human H2F light chain. At framework positions where the computer model suggested significant contact with the CDRs, the amino acids from the mouse antibody were substituted for the original human framework residues."

It appears that the instant "3D1" is the same as the "HF2.3D1" B7-2-specific antibody of the prior art. This reference differs from the instant invention by not disclosing the particular amino acid or nucleic acids of the HF2.3D1/ 3D1 antibody , nor of the particular "H2F", "I2R" antibodies and the "CRL-12524 cell line per se.

However, as clearly taught by Freeman et al.;, it was obvious to one of ordinary skill in the art at the time the invention was made to humanize various antibodies, including "HF2.3D1" B7-2-specific antibody, particularly in view of its specificity and functional properties known at the time the invention was made.

Given the availability of the HF2.3D1/ 3D1 antibody and hybridoma together to others with general immunoglobulin gene cloning and expression strategies, it would have been have been a matter of routine experimentation well within the ordinary skill level of art to generate chimeric or humanized HF2.3D1/ 3D1 antibody B7-2-specific antibodies, nucleic acids encoding said antibodies, vectors, host cells, methods of making and compositions thereof. Given the highly conserved nature of immunoglobulin gene organization and structure and the availability of probes and PCR primers for immunoglobulin gene cloning, one of ordinary skill in the art could have isolated the functionally rearranged heavy and light chain variable regions from the HF2.3D1 hybridoma cell line and determined their sequences with a complete expectation of success. For example, the ordinary artisan does not need to determine the amino acid sequences of a rearranged V (variable) region before cloning. The claims do not differ unexpectedly or unobviously from what one of ordinary skill in the art would have expected to obtain given the known HF2.3D1 hybridoma thereof, the known heavy and light chain and the art known techniques regarding the production of chimeric antibodies, as acknowledged by the number of available art known procedures disclosed in the instant specification and cited on the Information Disclosure Statement. The claimed DNA sequences must encode a recombinant antibody comprising heavy and/or light chain variable regions of the instant B7-2-specific antibodies.

It is noted Examples 1/II/III of the specification discloses that the design of the instant "3D1", "H2F", "I2R" antibodies and the "CRL-12524 cell line were humanized versions (and associated nucleic acids, vectors, hosts cells) of the "3D1"/B7-2-specific antibody. Furthermore, it is acknowledged that the modifications of "3D1" antibody were designed on known parameters, techniques and computer programs (ABMOD and ENCODE) at the time the invention was made (also see 1449 references), including modifications to the framework regions to allow the recombinant antibodies to maintain substantial affinity to B7-2. Therefore, the claims limitations were expected functional products and modifications of making and preparing humanized HF2.3D1 /B7-2-specific antibodies at the time the invention was made.

Immunoglobulin gene structure and organization were well understood in the art a the time the claimed invention was made and that strategies for cloning the DNAs encoding immunoglobulin variable regions genes were well established in the art at the time the claimed invention was made, as were methods for the production of DNA constructs encoding immunoglobulin variable regions. In addition, it was known at the time the invention was made that the benefits of producing recombinant antibodies to reduce the immunogenicity of therapeutic and diagnostic antibodies in human patients. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and admitted prior art, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, Ph.D.
Primary Examiner
Technology Center 1600
November 21, 2002